REMARKS/ARGUMENTS

Claims 1-2, 4-616, 19-29, 31, 32, and 35-37 are active in this application.

Non-elected species are retained as reconsideration of that election is still ongoing (see page 3 of the Official Action)

The claims are amended to define the diseases or disorders being treated in accordance with the evidence provided (and discussed below) in relation to the PI3K-gamma kinase.

In the Official Action, the Examiner has maintained that the claims are not enabled for the prophylaxis and/or treatment of any and all of the diseases listed in, for example, Claim 1. The Examiner has modified this rejection to concede that at least the treatment of inflammation is enabled (see page 3 of the Action). While Applicants appreciate that indication, in light of the additional evidence provided and discussed below, reconsideration of the rejection as it pertains to the amended claims is requested.

The MPEP makes the following statement regarding what constitutes "undue experimentation":

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde,* 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). See also *United States v. Telectronics, Inc.,* 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) ("The test of enablement is whether one reasonably skilled in the

art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.").

The claims of this application based on the use of compound according to formula I which are azolidinone-vinyl fused-benzenes. The listing of diseases is described in the specification as linked to the activity with the PI3k gamma lipid kinase. Indeed the specification in the Background section of the invention provides a lengthy discussion as to how the PI3k gamma functions as well as its involvement in cell signal.

As the target P13K gamma is a well-validated target in pharmaceutical research the compounds and its use in the diseases claimed is enabled.

This holds true even in the absence of specific dose regimens for treatment or prophylaxis. Considering the significance of the finding of a group of compounds that are active on P13K gamma, it appears not well balanced that the applicant is required to provide all details of the administration. Further, it is routine in the medical field to optimize dosages based on the disease, severity, gender, race, age among a host of other factors facing the individual patient.

Thus, further experimentation cannot be considered an undue burden.

Applicants submit a number of documents that support the fact that the target P13K gamma is effective for the treatment of the diseases claimed. That is, as P13K gamma is an effective target for treating the diseases identified in the claims and that the specification provides evidence that the azolidinone-vinyl fused-benzenes defined in the claims modulate the P13K gamma activity provides the necessary enabling disclosure of the methods as claimed in this application.

The Examiner maintained the rejections, in part, on the nature of the previously submitted documents as not specific of the Pi3Kγ. While that information is probative as the

documents related to Pi3K, the following additional documentation specifically discusses the gamma Pi3K.

For instance, see the general review about the high potential of Pi3Kgamma inhibition in the treatment of various human diseases like inflammatory/autoimmune conditions (SLE, psoriasis, rheumatoid arthritis) allergic (asthma), cardiovascular disorders: Pi3Kγ inhibition: towards an "aspirin of the 21st century"? Ruckle et al. Nature Reviews, Vol 5, Novembe r2006, 903-91 8. This review, as well as the included references, explains the specificity and the various roles that Pi3Kγ plays into several biological processes.

Additionally, the following more specific references are provided, which specify the role of Pi3Kγ in inflammatory and autoimmune disorders as well as in cardiovascular, platelet aggregation, lung injury and viral infections:

1. In addition to the role in inflammatory diseases, Pi3Kγ also plays a role in oncology, as described by C. Johnson et al., Oncogenes, 2007, 26, 7049-7057.
2. Pi3Kγ is also active in cardiovascular diseases by modulating heart muscle contractility or in hypertensive response: see Michael Crackower et al., Cell, Vol. 110, 737-749, September 20, 2002; Vecchione, Journal of Experimental Medicine, Vol 201, No 8, April 18 2005, 1217-1 228; and Petrucco et al., Cell. Vol. 118, 375-387, August 6 2004, 376-387
3. Pi3Kγ is known to be active in Lung injury, see Ho-Kee Yum The Journal of Immunology. 2001, 167, 6601-6608 (in particular page 6607)
4. P13Kγ is also known to be active in platelet aggregation, see Emillo Hirsch et al., FASEB Journal, Vol 15 Sept. 2001, 2019-2021
5. Pi3Kγ is involved in response to viral infection and inhibition of Pi3Kγ can indeed have global immunosuppressive effect, see Amanda M. et al., The Journal of Immunology, 2008, 180: 208 1-2088. Thus, Pi3Kγ clearly plays a

role in graft rejection. Specifically, modulation of P13Kγ is useful for the treatment of multiple sclerosis.

The relevant factors set forth in the *In re Wands* case are outlined in the Action, see also In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement). Moreover, the court cautioned that it is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. 858 F.2d at 737, 740, 8 USPQ2d at 1404, 1407.

First with regard to the "state of the prior art", the "level of skill in the art", and the "predictability of the art", Applicants make it clear that the compounds used in the claimed methods needed to practice the invention are described in the application. The tools for making those are within the skill in the field. As evidenced by the attached documentation, the additional references provided here demonstrate the correlation between PiKγ activity to the claimed diseases.

All of these factors ultimately relate to the final factor, namely, what level or "quantity of experimentation" is needed to practice the invention. As explained through the detailed description of the invention all that is required of one of ordinary skill in the art by the claimed invention is to use a compound to treat one of those disorders according to the ordinary practice of a clinician treating, e.g., a patient under his or her care.

It is noted that in the *In re Wands* case the Court ultimately held that the specification was enabling with respect to the claims at issue because "there was considerable direction and guidance" in the specification; there was "a high level of skill in the art at the time the

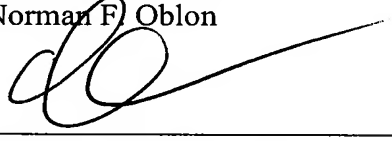
application was filed;" and "all of the methods needed to practice the invention were well known." 858 F.2d at 740, 8 USPQ2d at 1406. In the current case the "prior art" contains the correlative information needed to practice the invention coupled with the specific disclosure in the application relating to the compounds and their activity, there is "a high level of skill in the art" as conceded in the Action, and thus, the claims cannot be said to be not enabled. In light of the above, Applicants respectfully submit that the rejection under 35 U.S.C. § 112 ¶ 1, for lack of enablement should be withdrawn on the basis that an analysis of all the relevant factors under *In re Wands* clearly cannot support the Examiner's allegation that "undue experimentation" would be required to practice the invention.

Should the Examiner have any questions or wish to discuss any aspect of this application, he is invited to contact the undersigned at the number listed below.

A Notice of Allowance is requested.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon



Daniel J. Pereira, Ph.D.
Registration No. 45,518

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 08/07)